UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

December 10, 2002

MEMORANDUM

Product Name: Abamectin Technical
EPA File Symbol: 72167-EN
DP Barcode: D285183
Case No: 071714
Submission: S620750
Chemical: 122804 Abamectin

Byron T. Backus
12/10/2002
12/13/2002

From: Byron T. Backus, Ph.D., Toxicologist
Technical Review Branch
Registration Division (7505C)

To: Thomas Harris/Meredith Laws, PM 04
Insecticide-Rodenticide Branch
Registration Division (7505C)

Registrant: NATIONS AG II, LLC

ACTION REQUESTED: "AVERMECTIN (new source)

"Please review product tox data AND also determine if similar to existing registered tech (100-895). MRIDS: 455440-03 to -08."

BACKGROUND: According to the label received by TRB, this product [NATIONS AG II ABAMECTIN TECHNICAL] has the following ingredient declaration:

Active Ingredient:
Abamectin (CAS No. 65195-55-3 and CAS No. 65195-56-4):.....97.6%
Inert Ingredients:.....2.4%

oral LD50 in rats (MRID 45544003); acute dermal LD50 in rats (MRID 45544004); acute inhalation LC50 in rats (MRID 45544005); primary eye irritation in rabbits (MRID 45544006); primary dermal irritation in rabbits (MRID 45544007), and dermal sensitization in guinea pigs (MRID 45544008).

COMMENTS AND RECOMMENDATIONS:

1. The six submitted acute toxicity studies (MRIDs 45544003 through 45544008) have been reviewed and have been classified as acceptable.

2. Based on the results of the reviewed acute toxicity studies, the following is the acute toxicity profile for EPA File Symbol 72167-EN, Abamectin Technical:

Acute Oral LD50	Acceptable	Tox. Cat. II (MRID 45544003)
Acute Dermal LD50	Acceptable	Tox. Cat. II (MRID 45544004)
Acute Inhalation LC50	Acceptable	Tox. Cat. II (MRID 45544005)
Primary Eye Irritation	Acceptable	Tox. Cat. III (MRID 45544006)
Primary Dermal Irritation	Acceptable	Tox. Cat. IV (MRID 45544007)
Dermal Sensitization	Acceptable	Negative (MRID 45544008)

3. From the toxicity studies indicated above, the tentative signal word is WARNING, as the product is in toxicity category II by the acute oral, dermal and inhalation exposure routes. Note that according to the memorandum dated September 5, 2002 (copy attached), from Kathleen C. Raffaele of RAB3 of HED additional studies are required, and the findings from these may impact on the final precautionary labeling of this product.

4. Based on the acute toxicity profile given above and based on the proposed label use directions, the following is the tentative precautionary labeling for this product, as obtained from the Label Review System:

PRODUCT NAME: NATIONS AG II ABAMECTIN TECHNICAL

PRECAUTIONARY STATEMENTS

SIGNAL WORD: WARNING

Hazards to Humans and Domestic Animals:

May be fatal if swallowed, absorbed through skin, or if inhaled. Causes moderate eye irritation. Do not get in eyes, on skin, or on clothing. Wash thoroughly with soap and water after handling and before eating, drinking or using tobacco. Wear long-sleeved shirt and long pants, socks, chemical-resistant footwear, and gloves. Remove and wash contaminated clothing before reuse. Do not breathe dust. Wear a mask or pesticide respirator jointly approved by the Mine Safety and Health Administration and the National Institute for Occupational Safety and Health.

First Aid:

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

If inhaled:
-Move the person to fresh air.
-If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible.
-Call a poison control center or doctor for further treatment advice.

If swallowed:
-Call a poison control center or doctor immediately for treatment advice.
-Have person sip a glass of water if able to swallow.
-Do not induce vomiting unless told to by a poison control center or doctor.
-Do not give anything to an unconscious person.

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

NOTE TO PHYSICIAN: Note to PM/CRM/Registrant: The proposed label should contain a "Note to Physician". The following statements are suggested types of information that may be included, if applicable: - technical information on symptomatology; - use of supportive treatments to maintain life functions; - medicine that will counteract the specific physiological effects of the pesticide; - company telephone number to specific medical personnel who can provide specialized medical advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (870.1100, formerly §81-1)

Product Manager: 04
MRID No.: 45544003

Reviewer: Byron T. Backus, Ph.D.

CITATION: Moore, G.E. Abamectin Technical Acute Oral Toxicity Study in Rats. Laboratory Study No. 10833. Unpublished study prepared by Product Safety Labs, East Brunswick, NJ 08816. Study Completion Date: September 20, 2001. MRID 45544003.

SUBMITTER & SPONSOR: NATIONS AG II, LLC, Williamsburg, VA

TEST MATERIAL: Abamectin Technical, Batch #20010202, identified as containing 95% Abamectin and 5% other ingredients. An off-white powder. Certificate of analysis not provided by sponsor.

SPECIES: Rat, albino, Sprague-Dawley derived
AGE(at dosing): young adult, 9-10 weeks
WEIGHT (fasted): Males: 230-243 g; Females: 157-200 g
SOURCE: Ace Animals, Inc., Boyertown, PA

EXECUTIVE SUMMARY: ***In an acute oral toxicity study (MRID 45544003), fasted (approximately 19-20 hrs) young adult (9-10 week old) albino Sprague-Dawley derived rats (5 males and/or 5 females/dose level) were orally gavaged with abamectin technical, an off-white powder containing 95% abamectin and 5% other ingredients. The test material was administered as a 1% w/w suspension in a 2% w/w carboxymethyl cellulose (CMC) in distilled water at 50 mg/kg, and as a 30% w/w suspension in 2% CMC in distilled water for 500 mg/kg. Doses were 50 (females only) and 500 mg/kg. There were no mortalities in the 5 females dosed at 50 mg/kg; at 500 mg/kg 2/5 males and 5/5 females died.***

At 50 mg/kg, 2/5 rats were active and healthy throughout the 14-day observation period. 3/5 rats showed reduced fecal volume (from Day 1 to, in one case, Day 5), while one of these rats also showed hunched posture (Days 1-2), hypoactivity (Days 1-3), and facial staining (Days 2-5). All rats appeared normal from Day 6 to Day 14.

At 500 mg/kg, symptoms in 2/5 males were limited to hypoactivity on Day 1. Symptoms in the other 3 rats included hypoactivity, facial staining, tremors, hunched posture and irregular respiration, with one of these males dying on Day 2 and one dying on Day 6. The remaining animal had recovered by Day 7. All 5 females dosed at 500 mg/kg died in the period from Day 1 to Day 9. Symptoms in these females included hypoactivity, prone [position or lateral recumbency?], tremors, facial staining, hunched posture, red ocular discharge, irregular respiration (with dyspnea and gasping in one animal).

Gross pathological findings in the rats which died included moderately red lungs (5/7), black, black-red or red intestines (7/7), discolored liver (1/7) and ano-genital staining (1/7). There were no gross abnormalities in the rats which survived to termination.

Oral LD50 Males > 500 mg/kg
Oral LD50 Females > 50 mg/kg but <500 mg/kg

Abamectin technical, and off-white powder containing 95% abamectin and 5% other ingredients is in toxicity category II for oral toxicity based on the female oral LD50 value.

Study Classification: Acceptable

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 20), and [No] Data Confidentiality (p. 2) statements were provided.

Procedure (including deviations from 870.1100): The test material was administered as a 1% w/w suspension in 2% w/w carboxymethyl cellulose (CMC) in distilled water for the 50 mg/kg dose level and as a 30% w/w suspension in 2% CMC in distilled water for the 500 mg/kg dose level. "Prior to dosing, each group of animals was fasted for approximately 19-20 hours... Each animal received the appropriate amount of the test substance...by intubation using a stainless steel ball-tipped gavage needle attached to an appropriate syringe... The day of administration was considered Day zero of the study."

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Total
50	-	0/5	0/5
500	2/5	5/5	7/10

Observations: At 50 mg/kg, 2/5 rats were active and healthy throughout the 14-day observation period. 3/5 rats showed reduced fecal volume (from Day 1 to, in one case, Day 5), while one of these rats also showed hunched posture (Days 1-2), hypoactivity (Days 1-3), and facial staining (Days 2-5). All rats appeared normal from Day 6 to Day 14.

At 500 mg/kg, symptoms in 2/5 males were limited to hypoactivity on Day 1. Symptoms in the other 3 rats included hypoactivity, facial staining, tremors, hunched posture and irregular respiration, with one of the these males dying on Day 2 and one dying on Day 6. The remaining animal had recovered by Day 7. All 5 females dosed at 500 mg/kg died in the period from Day 1 to Day 9. Symptoms in these females included hypoactivity, prone [position or lateral recumbency?], tremors, facial staining, hunched posture, red ocular discharge, irregular respiration (with dyspnea and gasping in one animal).

Gross Necropsy: Gross pathological findings in the rats which died included moderately red lungs (5/7), black, black-red or red intestines (7/7), discolored liver (1/7) and ano-genital staining (1/7). There were no gross abnormalities in the rats which survived to termination.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (870.1200, formerly §81-2)

Product Manager: 04 **Reviewer:** Byron T. Backus, Ph.D.
MRID No.: 45544004

CITATION: Moore, G.E. Abamectin Technical Acute Dermal Toxicity Study in Rats. Laboratory Study No. 10834. Unpublished study prepared by Product Safety Labs, East Brunswick, NJ 08816. Study Completion Date: September 20, 2001. MRID 45544004.

SUBMITTER & SPONSOR: NATIONS AG II, LLC, Williamsburg, VA 23185

TEST MATERIAL: Abamectin Technical, Batch #20010202, identified as containing 95% Abamectin and 5% other ingredients. An off-white powder. Certificate of analysis not provided by sponsor.

SPECIES: Rat, albino, Sprague-Dawley derived
AGE(at dosing): young adult, 8-10 weeks
WEIGHT: Males: 202-264 g; Females: 170-215 g
SOURCE: Ace Animals, Inc., Boyertown, PA

EXECUTIVE SUMMARY: ***In an acute dermal toxicity study (MRID 45544004), groups of 5M & 5F young adult (8-10 weeks old) albino Sprague-Dawley derived rats were dermally exposed for 24 hrs (occluded exposure) to doses of 200, 2000 and 5000 mg/kg abamectin technical, an off-white powder containing 95% abamectin and 5% other ingredients. The test material was applied as a 60% w/w mixture in distilled water.***

At the two highest dose levels (2000 & 5000 mg/kg) all rats (5M & 5F/dose) died. At 200 mg/kg all rats survived. Symptoms occurred at all dose levels; at 200 mg/kg 2/5 males showed tremors, 3/5 showed hypoactivity and 1/5 had facial staining; 2/5 males showed no symptoms at all. Males with symptoms recovered by Day 7. For 200 mg/kg females, 5/5 showed hypoactivity, 3/5 had tremors, and 1/5 had facial staining and 2/5 had reduced fecal volume. All females had recovered by Day 12. At 2000 mg/kg deaths occurred from Day 2 to Day 7. Symptoms included hypoactivity, tremors, exophthalmos, irregular respiration and gasping. At 5000 mg/kg deaths occurred from Day 2 to Day 6; most symptoms were the same as at 2000 mg/kg, but additional observations in some rats included prolapsed tongue, red oral discharge and ano-genital staining.

No gross abnormalities were found on post-sacrifice necropsy in rats which had been dosed at 200 mg/kg; at 2000 mg & 5000 mg/kg observations included moderately to extremely red lungs, discolored liver, dark red or red intestines.

Dermal LD50 Males > 200 mg/kg (0/5 died at this dose level); < 2000 mg/kg (5/5 died)
Dermal LD50 Females > 200 mg/kg (0/5 died at this dose level); < 2000 mg/kg (5/5 died)
Combined > 200 mg/kg (0/10 died at this dose level); < 2000 mg/kg (10/10 died)

Abamectin technical, an off-white powder containing 95% abamectin and 5% other ingredients, is in toxicity category II in terms of dermal toxicity.

Study Classification: Acceptable

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 24), and [No] Data Confidentiality (p. 2) statements were provided.

Procedure (including deviations from 870.1200): "On the day before application, each group of animals was prepared by clipping the dorsal area and the trunk... Prior to application, the test substance was moistened with distilled water to achieve a dry paste by preparing a 60% w/w mixture. The appropriate amount of test substance (200, 2,000 or 5,000 mg/kg of bodyweight) was then evenly applied over a dose area of approximately 2 inches x 3 inches (approximately 10% of the body surface) and covered with a 2 inch x 3 inch, 4-ply gauze pad. The gauze pad and entire trunk of each animal were then wrapped with 3 inch Durapore tape to avoid dislocation of the pad and to minimize loss of the test substance... After 24 hours of exposure to the test substance, the pads were removed and the test sites gently rinsed with water and wiped with a clean towel to remove any residual test substance."

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
200	0/5	0/5	0/10
2000	5/5	5/5	10/10
5000	5/5	5/5	10/10

Observations: All animals survived at 200 mg/kg; all animals exposed to 2000 and 5000 mg/kg dermal doses died. At 200 mg/kg most of the rats "exhibited clinical signs including facial staining, hypoactivity, prone posture, tremors and/or a reduced fecal volume, but recovered by study termination [all males had recovered by Day 7, all but one female had recovered by Day 6 and the remaining female recovered by Day 12]. Although one female lost bodyweight through Day 7, all animals gained weight over the entire 14-day observation period,

At 2000 mg/kg: "Toxic signs noted prior to death included ocular discharge, abnormal respiration, hypoactivity, prone posture, tremors, exophthalmos and/or emaciation..."

At 5000 mg/kg: "Toxic signs noted prior to death included ocular, nasal or oral discharge, facial staining, irregular respiration, hypoactivity, prone posture, tremors, ano-genital staining and/or a prolapsed tongue..."

Gross Necropsy: 200 mg/kg: "No gross abnormalities were noted for the animals when necropsied at the conclusion of the study."

2000 mg/kg: "Gross necropsy of the decedents revealed discoloration of the lungs, liver and/or intestines, gaseous distention of the intestines and/or rigor mortis."

5000 mg/kg: "Gross necropsy of the decedents revealed discoloration of the small intestines and/or lungs. Additional necropsy findings included facial staining, ano-genital staining, a prolapsed tongue and/or rigor mortis."

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (870.1300, formerly §81-3)

Product Manager: 04
MRID No.: 45544005

Reviewer: Byron T. Backus, Ph.D.

CITATION: Moore, G.E. Abamectin Technical Acute Inhalation Toxicity Study in Rats. Laboratory Study No. 10835. Unpublished study prepared by Product Safety Labs, East Brunswick, NJ 08816. Study Completion Date: October 31, 2001. MRID 45544005.

SUBMITTER & SPONSOR: NATIONS AG II, LLC, Williamsburg, VA 23185
TEST MATERIAL: Abamectin Technical, Batch #20010202, identified as containing 95% Abamectin and 5% other ingredients. An off-white powder. Certificate of analysis not provided by sponsor.
SPECIES: Rat, albino, Sprague-Dawley derived
AGE(at exposure): young adult, 8-9 weeks
WEIGHT (at exposure): Males: 203-275 g; Females: 174-205 g
SOURCE: Ace Animals, Inc., Boyertown, PA

EXECUTIVE SUMMARY: ***In an acute inhalation toxicity study (MRID 45544005), groups of 5 male and 5 female young adult (8-9 weeks old) Sprague-Dawley rats received 4-hour exposures to mean concentrations of 0.21 mg/L (whole body exposure), 0.053 mg/L (whole body exposure) and 0.055 mg/L (nose-only exposure) Abamectin technical, an off-white powder identified as containing 95% abamectin and 5% other ingredients. Prior to aerosolization the test material was ground in a ball mill for 24 hours. In the whole body exposure with 0.053 mg/L the MMAD was 2.8 μm (mean GSD = 2.11), and in the nose-only exposure with 0.055 mg/L the MMAD was 2.65 μm (mean GSD = 1.98).***

In the nose-only exposure at 0.055 mg/L 1/5 males and 0/5 females died. The one rat which died apparently did so during exposure. All the remaining rats in this group showed symptoms (such as hypoactivity, ventral staining, hunched posture, ocular discharge and irregular respiration; 1/5 males and 1/5 females showed tremors) at the time of removal from the exposure chamber, with recovery by Day 4. In the whole body exposure at 0.053 mg/L 3/5 M and 4/5 females died in the period from Day 1 to Day 5. Symptoms included prone position, tremors, hypoactivity, irregular respiration, hunched posture, dyspnea, protruding tongue and exophthalmos. The 3 survivors recovered by Day 11. At 0.21 mg/L (whole body exposure) all animals died by Day 5 with symptoms similar to those of rats at the lower dose levels.

The rat dying in nose-only exposure at 0.055 mg/L had slightly red, edematous lungs. All other rats in this group had no gross abnormalities at post-sacrifice necropsy. At 0.053 mg/L (whole body exposure) findings in rats which died included dark mottled red or red lungs, discoloration of the small intestines and/or liver. The three rats which survived to sacrifice had no gross abnormalities. At 0.21 mg/L whole body exposure necropsy findings included mottled red lungs with edema in all rats, with two showing red or black-red intestines.

Inhalation LC50 Males > 0.055 mg/L (1/5 died with nose-only exposure)
Inhalation LC50 Females > 0.055 mg/L (0/5 died with nose-only exposure)
Combined LC50 > 0.055 mg/L (1/10 rats died)

Abamectin technical, identified as containing 95% abamectin and 5% other ingredients, is in toxicity category II in terms of acute inhalation toxicity, based on the LC50 > 0.055 mg/L under nose-only exposure conditions.
Study Classification: Acceptable

COMPLIANCE: Signed and dated GLP (p. 3), Quality Assurance (p. 38) and [No] Data Confidentiality (p. 2) statements are provided.

Procedure (including deviations from 870.1300): "Prior to aerosolization, the test substance was ground in a ball mill for 24 hours... [The test substance was processed in a urethane-lined milling jar with porcelain grinding media (0.5" balls) for 24 hours. After milling, the test substance was sieved through a 3/8" polyethylene sieve...]

"Initially, exposure levels of 0.05 and 0.2 mg/L were selected for testing. Animals were exposed to the test atmosphere in a whole body inhalation chamber for 4 hours. The mortality noted in these two test groups was higher than expected. Based on the results of the oral and dermal toxicity studies...it appeared that exposure via the oral and dermal route during whole body exposure may have contributed to the overall toxicity noted in the inhalation study.

"To further evaluate this possibility, a third exposure was conducted at a targeted exposure level of 0.05 mg/L using a nose-only exposure chamber..."

Results:

Mean Exposure Concentration mg/L (Gravimetrically Determined)	Number of Deaths/Number Tested		
	Males	Females	Combined
0.053 (whole-body exposure)	3/5	4/5	7/10
0.055 (nose-only exposure)	1/5	0/5	1/10
0.21 (whole-body exposure)	5/5	5/5	10/10

The nominal concentrations were 0.19 mg/L (0.053 mg/L whole-body exposure), 0.14 mg/L (0.055 mg/L nose-only exposure), and 0.68 mg/L (0.21 mg/L whole-body exposure).

Clinical Observations: At 0.053 mg/L whole-body exposure 3/5 males and 4/5 females died. Deaths occurred in the period from Day 1 to Day 5, with most deaths (5) occurring on Day 2. "In-chamber animal observations included ocular and nasal discharge, irregular respiration, hunched posture, hypoactive [hypoactivity?] and tremors. Upon removal from the exposure chamber, all animals continued to exhibit similar clinical signs and also developed a prone posture, gasping, facial staining, exophthalmos, a protruding tongue, dyspnea and/or reduced fecal volume. The three surviving animals recovered from the above symptoms by Day 11 and appeared active and healthy for the remainder of the study. Although all three survivors lost bodyweight between Days 0 and 7, all gained weight over the entire 14-day observation period."

At 0.055 mg/L nose-only exposure: One male died. "Upon removal from the exposure tubes, one rat was found dead. All surviving animals exhibited clinical signs including ocular and nasal discharge, irregular respiration, hypoactivity, hunched posture, tremors and/or ventral staining. All survivors recovered from the above symptoms by Day 4 and appeared active and healthy for the remainder of the study, gaining bodyweight over the 14-day observation period." From information on page 30 of MRID 45544005 all survivors gained weight in the periods from Day 0 to Day 7 and again in the period from Day 7 to Day 14.

At 0.21 mg/L whole-body exposure: Eight of the ten deaths occurred on Days 0-1, the remaining two deaths (in two males) occurred on Day 5. "All animals died as a result of exposure to the test

atmosphere... In-chamber animal observations included ocular and nasal discharge, irregular respiration, hunched posture, hypoactivity and tremors. Upon removal from the exposure chamber, two animals were found dead. Prior to death, the remaining animals continued to exhibit similar clinical signs and also developed facial staining, a prone posture and/or a reduced fecal volume."

Gross Necropsy: At 0.053 mg/L whole-body exposure: "Gross necropsy of the decedents revealed discoloration of the lungs, liver and/or intestines, rigor mortis, ano-genital staining, oral and ocular discharge. The trachea of one animal also contained an off-white solid. No gross abnormalities were noted for the surviving animals necropsied at the conclusion of the study (Day 14)."

At 0.055 mg/L nose-only exposure: "Gross necropsy of the decedent revealed discoloration and edema of the lungs. No gross abnormalities were noted for the surviving animals necropsied at the conclusion of the study (Day 14)."

At 0.21 mg/L whole-body exposure: "Gross necropsy of the decedents revealed rigor mortis, edema of the lungs and discoloration of the intestines and/or lungs."

Chamber Atmosphere		
Grav. Conc. (mg/L)	**MMAD (µm)**	**Mean GSD**
0.053	2.8	2.11
0.055	2.7	1.98
0.21	2.9	2.00

Particle Size Distribution: At 0.055 mg/L >61% of the particles by weight had an effective cut-off diameter of 3.3 µm or less, and > 78% had an effective cut-off diameter of 4.7 µm or less.

Chamber Environment (0.053 & 0.21 mg/L whole-body exposure)	
Internal Chamber Volume	100 L
Mean Airflow (inlet)	50.6 LPM
Mean Temperature	21-24°C
Mean Relative Humidity	52-70%

Chamber Environment (0.055 mg/L nose-only exposure)	
Internal Chamber Volume	6.7 L
Mean Airflow (inlet)	31.6 LPM
Mean Temperature	21-22°C
Mean Relative Humidity	60-68%

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (870.2400, formerly §81-4)

Product Manager: 04
MRID No.: 45544006

Reviewer: Byron T. Backus, Ph D.

CITATION: Moore, G.E. Abamectin Technical Primary Eye Irritation Study in Rabbits. Laboratory Study Identification No. 10836. Unpublished study prepared by Product Safety Labs, East Brunswick, NJ 08816. Study Completion Date: September 20, 2001. MRID 45544006.

SUBMITTER & SPONSOR: NATIONS AG II, LLC, Williamsburg, VA 23185

TEST MATERIAL: Abamectin Technical, Batch #20010202, identified as containing 95% Abamectin and 5% other ingredients. An off-white powder. Certificate of analysis not provided by sponsor.

SPECIES: Rabbit, New Zealand White (2 males and 1 female used)
AGE: "young adult"
WEIGHT: not stated
SOURCE: Davidson's Mill Farm, South Brunswick, NJ

EXECUTIVE SUMMARY: ***In a primary eye irritation study (MRID 45544006), 0.1 mL (approximately 0.05 to 0.06 g) of Abamectin technical, an off-white powder identified as containing 95% Abamectin and 5% other ingredients, was instilled into one eye of each of 3 young adult New Zealand white rabbits.***

All 3 eyes scored "1" (not considered a positive response) for conjunctival redness at 1 hour, and this was the maximum conjunctival redness observed (2/3 scored "1" at 24 hours and 1/3 scored "1" at 48 hours). However, one eye scored "1" (a positive response) for corneal irritation at 24 hours; this had cleared by 48 hours. All scores were zero at 72 hours.

The test material, Abamectin technical, an off-white powder identified as containing 95% Abamectin and 5% other ingredients, is in toxicity category III in terms of primary eye irritation potential, based on the presence of corneal opacity in 1/3 eyes at 24 hours which had cleared by 48 hours.

Study Classification: Acceptable

COMPLIANCE: Signed and dated GLP (p. 3), Quality Assurance (p. 15) and [No] Data Confidentiality (p. 2) statements are provided.

Procedure (including deviations from 870.2400): "One-tenth of a milliliter (approximately 0.05 to 0.06 grams) was instilled into the conjunctival sac of the right eye of each rabbit by pulling the lower lid away from the eyeball. The upper and lower lids were then gently held together for about one second before releasing to minimize loss of the test substance..."

Results:

Observations	Number scoring positive/total number			
	1 hr	24 hrs	48 hrs	14 days
Corneal Opacity	0/3	1/3[b]	0/3	0/3
Iritis	0/3	0/3	0/3	0/3
Conjunctivae:				
Redness[a]	0/3	0/3	0/3	0/3
Chemosis[a]	0/3	0/3	0/3	0/3
Discharge[a]	0/3	0/3	0/3	0/3

[a]Score of 2 or more considered positive.
[b]One drop of ophthalmic fluorescein sodium was instilled into the eye to evaluate the presence and extent of corneal damage.

All 3 eyes scored "1" (not considered a positive response) for conjunctival redness at 1 hour, and this was the maximum conjunctival redness observed (2/3 scored "1" at 24 hours and 1/3 scored "1" at 48 hours). However, one eye scored "1" (a positive response) for corneal irritation at 24 hours; this had cleared by 48 hours. All scores were zero at 72 hours.

DATA REVIEW FOR PRIMARY DERMAL IRRITATION TESTING (870.2500, formerly §81-5)

Product Manager: 04
MRID No.: 45544007

Reviewer: Byron T. Backus, Ph.D.

CITATION: Moore, G.E. Abamectin Technical Primary Skin Irritation Study in Rabbits. Laboratory Study Identification No. 10837. Unpublished study prepared by Product Safety Labs, East Brunswick, NJ 08816. Study Completion Date: September 20, 2001. MRID 45544007.

SUBMITTER & SPONSOR: NATIONS AG II, LLC, Williamsburg, VA 23185

TEST MATERIAL: Abamectin Technical, Batch #20010202, identified as containing 95% Abamectin and 5% other ingredients. An off-white powder. Certificate of analysis not provided by sponsor.

SPECIES: Rabbit, albino, New Zealand White (2 males and 1 female used)
AGE: "young adult"
WEIGHT: not stated
SOURCE: Davidson's Mill Farm, South Brunswick, NJ

EXECUTIVE SUMMARY: ***In a dermal irritation study (MRID 45544007), 0.5 g of Abamectin Technical, an off-white powder identified as containing 95% Abamectin and 5% other ingredients, was applied (as a 70% w/w mixture in distilled water) to an intact skin site on the back of each of 3 New Zealand white rabbits, with 4-hr semi-occluded exposure.***

There was no irritation; all scores for erythema and edema were zero at 1, 24, 48 and 72 hours. The Primary Irritation Index (average of 1, 24, 48 and 72 hour scores) = 0.00. The test material, Abamectin Technical, an off-white powder identified as containing 95% Abamectin and 5% other ingredients is in toxicity category IV in terms of primary skin irritation potential.

Study Classification: Acceptable

COMPLIANCE: Signed and dated GLP (p. 3), Quality Assurance (p. 15) and [No] Data Confidentiality (p. 2) statements were provided.

Procedure (including deviations from 870.2500): "Prior to application, the test substance was moistened with distilled water to achieve a dry paste by preparing a 70% w/w mixture. Five-tenths of a gram of the test substance (0.71 g of the test mixture) was placed on a 1 inch x 1 inch, 4-ply gauze pad and applied to one 6 cm^2 intact dose site on each animal. The pad and entire trunk of each animal were then wrapped with semi-occlusive 3 inch Micropore tape to avoid dislocation of the pad. Elizabethan collars were placed on each rabbit... After 4 hours of exposure to the test substance, the pads and collars were removed and the test sites gently wiped with water and a clean towel to remove any residual test substance."

Results: There was no irritation; all scores for erythema and edema were zero at 1, 24, 48 and 72 hours. The Primary Irritation Index (average of 1, 24, 48 and 72 hour scores) = 0.00

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (870.2600, formerly §81-6)

Product Manager: 04
MRID No.: 45544008

Reviewer: Byron T. Backus, Ph.D.

CITATION: Moore, G.E. Abamectin Technical Dermal Sensitization Study in Guinea Pigs (Buehler Method). Laboratory Study Identification No. 10838. Unpublished study prepared by Product Safety Labs, East Brunswick, NJ 08816. Study Completion Date: September 20, 2001. MRID 45544008.

SUBMITTER & SPONSOR: NATIONS AG II, LLC, Williamsburg, VA 23185

TEST MATERIAL: Abamectin Technical, Batch #20010202, identified as containing 95% Abamectin and 5% other ingredients. An off-white powder. Certificate of analysis not provided by sponsor.

SPECIES: Guinea Pig, albino, Hartley, Females only (test group)
AGE(at initiation of induction): "Young adult"
WEIGHT(at initiation of induction): Females: 315-396 g
SOURCE: Elm Hill Breeding Labs, Chelmsford, MA

EXECUTIVE SUMMARY: ***In a dermal sensitization study (MRID 45544008) using a Buehler protocol, 20 young adult Hartley albino female guinea pigs each received a total of three six-hour occluded induction exposures, once a week for three weeks, to 0.4 g of an 80% w/w mixture of Abamectin technical (identified as containing 95% Abamectin and 5% other ingredients) and distilled water.***

Four weeks after the first induction dose, previously induced guinea pigs were challenged (at a previously unexposed dermal site), along with a previously unexposed control group of 10 female guinea pigs, to a 6-hr exposure to 0.4 g of an 80% w/w mixture of Abamectin technical (identified as containing 95% Abamectin and 5% other ingredients) and distilled water.

During induction, no irritation (all scores zero) was observed at either 24 or 48 hours following exposure. 2/20 guinea pigs died during this period, with symptoms (such as ocular discharge, tremors, irregular respiration, or hypoactivity) consistent with the toxicity of the test material. Some of the other guinea pigs also showed symptoms, particularly after the first induction treatment, but subsequently recovered.

At challenge 7/18 previously induced guinea pigs scored "0.5" at 24 hours and 2/18 scored "0.5" at 48 hours. 2/10 naive controls scored "0.5" at 24 hours and all scored zero at 48 hours. As "0.5" is not a positive response, it is concluded that the test material did not elicit a dermal sensitization reaction.

The report includes a positive control study which used 1-Chloro-2,4-Dinitrobenzene (DNCB) as the test material (with 0.08% w/w DNCB in 80% aqueous alcohol used for inductions, and 0.04% w/w DNCB in acetone used for challenge). The results were appropriate. This study was completed on December 21, 2000; it is noted that the first induction treatment with Abamectin technical was on or shortly after July 13, 2001. While this is slightly outside the six month period specified in the Guidelines, the conclusion has been made that this does not impact on the validity or acceptability of the study.

Study Classification: Acceptable. The findings of this study are consistent with a lack of dermal sensitization activity for the test material, Abamectin technical, an off-white powder identified as containing 95% Abamectin and 5% other ingredients.

COMPLIANCE: Signed and dated GLP (p. 3), Quality Assurance (p. 27) and [No} Data Confidentiality (p. 2) statements are provided.

Procedure: The dosages used for induction and challenge were based on preliminary irritation studies. For induction: "Once each week for three weeks, four-tenths of a gram of an 80% w/w mixture of the test substance in distilled water was applied to the left side of each test animal using an occlusive 25 mm Hill Top Chamber®. The chambers were secured in place and wrapped with non-allergenic Durapore adhesive tape to avoid dislocation of the chambers and to minimize loss of the test substance. After the 6-hour exposure period, the chambers were removed and the test sites were gently wiped with water and a clean towel to remove any residual test substance. Approximately 24 and 48 hours after each induction application, readings were made of local reactions (erythema)..."

For challenge:"Twenty-eight days after the first induction dose, four-tenths of a gram of an 80% w/w mixture [HNIC: Highest Non-Irritating Concentration, as determined in an irritation screen] of the test substance in distilled water was applied to a naive site on the right side of each animal as a challenge dose... These sites were evaluated for a sensitization response (erythema) approximately 24 and 48 hours after the challenge application... In addition to the [previously induced] test animals, 10 guinea pigs from the same shipment were maintained under identical environmental conditions and were treated with the HNIC of the test substance at challenge only..."

Results: During induction, no irritation (all scores zero) was observed at either 24 or 48 hours following exposure. 2/20 guinea pigs died during this period, with symptoms (such as ocular discharge, tremors, irregular respiration, or hypoactivity) consistent with the toxicity of the test material. Some of the other guinea pigs also showed symptoms, particularly after the first induction treatment, but subsequently recovered.

At challenge 7/18 previously induced guinea pigs scored "0.5" at 24 hours and 2/18 scored "0.5" at 48 hours. 2/10 naive controls scored "0.5" at 24 hours and all scored zero at 48 hours. As "0.5" is not a positive response, it is concluded that the test material did not elicit a dermal sensitization reaction.

The report includes a positive control study which used 1-Chloro-2,4-Dinitrobenzene (DNCB) as the test material (with 0.08% w/w DNCB in 80% aqueous alcohol used for inductions, and 0.04% w/w DNCB in acetone used for challenge). The results were appropriate. This study was completed on December 21, 2000; it is noted that the first induction treatment with Abamectin technical was on or shortly after July 13, 2001. While this is slightly outside the six month period specified in the Guidelines, the conclusion has been made that this does not impact on the validity or acceptability of the study.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D285183
2. **PC CODE:** 122804 Abamectin
3. **CURRENT DATE:** December 10, 2002
4. **TEST MATERIAL:** [EPA File Symbol: 72167-EN]; Abamectin Technical, Batch #20010202, identified as containing 95% Abamectin and 5% other ingredients. An off-white powder. Certificate of analysis not provided by sponsor.

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat/ Product Safety Labs/Lab Study No. 10833/SEP-20-2001	45544003	LD_{50}(M) > 500 mg/kg (2/5 died at this dose level); LD_{50}(F) > 50 mg/kg (0/5 died at this dose level; 5/5 died at 500 mg/kg). 2/5 females dosed at 50 mg/kg had no signs, but 3 had reduced fecal volume & one had hypoactivity, hunched posture and facial staining, with recovery by Day 6. At 500 mg/kg symptoms included irregular respiration, tremors, hunched posture. Surviving males normal by Day 7.	II	A
Acute dermal toxicity/rat/ Product Safety Labs/Lab Study No. 10834/SEP-20-2001	45544004	LD_{50} > 200 mg/kg (males, females, combined; no deaths at this exposure level); <2000 mg/kg (all rats died). Symptoms at 200 mg/kg: tremors, hypoactivity & facial staining with recovery by Day 7 for M and Day 12 for F.	II	A
Acute inhalation toxicity/ rat/ Product Safety Labs/ Lab Study No. 10835/ OCT-31-2001	45544005	LC_{50} > 0.055 mg/L by nose-only exposure (1/5 M, 0/5 F died following exposure at this level) with survivors recovering from symptoms (ocular & nasal discharge, irregular respiration, hypoactivity, hunched posture, tremors and/or ventral staining) by Day 4. MMAD = 2.7 µm; GSD = 1.98. At 0.053 mg/L by whole-body exposure 3/5M & 4/5F died; at 0.21 mg/L whole-body exposure 5/5M & 5/5F died.	II	A
Primary eye irritation/ rabbit/Product Safety Labs /Lab Study No. 10836/ SEP-20-2001	45544006	3 NZ white rabbit eyes exposed. 0.1 mL (0.05-0.06 g test material) instilled. One eye scored "1" for corneal opacity at 24 hours; all eyes were clear (all scores zero) by 72 hours.	III	A
Primary dermal irritation/ rabbit/Product Safety Labs /Lab Study No. 10837/ SEP-20-2001	45544007	PII (av. of 1, 24, 48 & 72 hr scores) = 0.00 with all scores zero. 0.5 g test material was moistened with distilled water to form a 70% w/w mixture.	IV	A

Dermal sensitization/ guinea pig/Product Safety Labs/Lab Study No. 10838 /SEP-20-2001	45544008	Buehler protocol: 20 Hartley albino females each received a total of 3 6-hr occluded exposures to 0.4 g of an 80% w/w mixture of Abamectin technical in distilled water. 4 weeks after first dose, survivors were challenged at a naive site, along with a control group of 10 females, to a 6-hr exposure of 80% w/w test material in distilled water. During induction 2/20 guinea pigs died with symptoms consistent with the toxicity of test material, but there was no dermal irritation. At challenge: 7/18 scored 0.5 at 24 hrs and 2/18 scored 0.5 at 48 hrs; all others scored zero. Controls: 2/10 scored 0.5 at 24 hrs and all scored zero at 48 hrs. Findings are consistent with a lack of dermal sensitization activity for test material.	Not a sensitizer	A

Core Grade Key: **A =Acceptable, S = Supplementary, U = Unacceptable, V = Self Validated**